F1 Contd

microstructures, cells, vesicles, microparticles, polymers, gels, matrices, blood forming elements, reticuloendothelial cells, liposomes, microspheres, nanostructures, biopolymers, multimolecular complexes, cell membranes, implants and prosthetic devices.

REMARKS

At the outset Applicant thanks Examiner Ware and Examiner Kishore for the Telephone Interview conducted on August 22, 2001 and for subsequent telephone discussions conducted thereafter on September 10th and October 9th.

Claims 13 through 29 are pending in the instant application. In an earnest effort to respond to Examiner Kishore's suggestion during the August 22nd Telephone Interview, Applicant has canceled pending claims 13-29, without prejudice, and added new claims 30-41 which include additional language in the claims relating to the steps by which synthetic receptors are selected and the prodrug and multi-prodrug complexes of the present invention are produced and administered. As discussed during the Telephone Interview, the additional language in the claims is being provided to assist Examiner Ware in more effectively searching the instant invention. Claims 30-41 are identical to the claims which Applicant faxed to

Examiner Ware on August 23, 2001 for consideration. From subsequent telephone conversations with Examiner Ware and Examiner Kishore, it is Applicant's understanding that the new claims provide the detail needed for Examiner Ware to effectively search the claimed invention.

Support for new claims 30-41 is provided throughout specification. In particular, the Examiner is respectfully directed to page 9, line 28, through page 10, line 25, wherein methods for selection of synthetic receptors are described. The Examiner is also respectfully directed to Examples 1 through 4 at pages 15 through 21 where use of these methods for selection of synthetic receptors and production of prodrug and multi-prodrug complexes of the present invention are illustrated in examples. Thus, no new matter is added by this amendment.

The differences between the instant invention and that taught by cited prior art of record, namely Morgan Jr. et al. (U.S. Patent 5,252,713), are even more clear in claims 30-41.

Claims 30-41 are drawn to methods of producing and administering a prodrug complex and to prodrug complexes and multi-prodrug complexes produced via these methods wherein the synthetic receptor of the complex is selected by either combinatorial selection (claim 30) or *in vitro* evolution (claim

32), or the synthetic receptor specifically binds the drug via a saturable, noncovalent interaction between the drug and the synthetic receptor that can be competitively inhibited by structural analogs of the drug and is from the group consisting of antibodies, antibody fragments, oligonucleotides and oligosaccharides (claim 34).

Morgan Jr. et al. provides no teaching or suggestion whatsoever with respect to selection of a synthetic receptor via combinatorial selection or *in vitro* evolution. Accordingly, this reference can neither anticipate nor render obvious new claims 30 or 32, or claims dependent therefrom.

Further, with respect to claim 34 and claims dependent therefrom, as discussed in great detail in the Preliminary Amendment filed by Applicant on May 3, 2001, the immunoconjugates of Morgan Jr. et al. comprise either a targeting protein such as an antibody or antibody fragment, a moiety termed a drug binding molecule of complementary structure (abbreviated csDBM) which is covalently bound to the antibody or carrier, and a drug noncovalently complexed to the csDBM (see col. 4, lines 61-67 of the '951 patent), or alternatively, a drug first bound through covalent bonds to an antibody or carrier and then complexed with a csDBM (see col. 4, line 67, through 5, line 2). In contrast, the

prodrug complexes produced in accordance with claim 34 and claims dependent therefrom do not contain a csDBM. Nor do the complexes of the present invention involve covalently binding a drug to an antibody or carrier and then complexing the drug with a csDBM. Instead, it is clearly stated in step (b) of claim 34 that the selected synthetic receptor specifically binds the drug via a saturable, noncovalent interaction between the drug and the synthetic receptor that can be competitively inhibited by structural analogs of the drug. Further, it is stated in the claim that the synthetic recepted is selected from the group consisting of antibodies, antibody fragments, oligonucleotides and oligosaccharides. Accordingly, new claim 34 makes clear that the csDBM, which is an essential component of the immunoconjugates of Morgan Jr. et al., is not a part of the instant invention.

Withdrawal of all pending rejections under 35 U.S.C. § 102 and 103 is therefore respectfully requested.

In addition, new claims 30-41 do not contain the language suggested to be indefinite under 35 U.S.C. § 112, second paragraph, by Examiner Ware in the Office Action dated June 5, 2001. Accordingly, withdrawal of this rejection is also respectfully requested.

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record and addresses all concerns raised in this Office Action as well as those raised by Examiner Kishore during the Telephone Interview of August 22, 2001. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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